Claims 1-108. (Cancelled)

Claim 109 (Currently amended) A molecular biosensor, the biosensor having two constructs, the constructs comprising:

R1-R2-R3-R4; and

R5-R6-R7-R8;

wherein:

R1 is an antibody epitope binding agent that binds to a first epitope on a target molecule;

R2 is a non-nucleic acid flexible linker attaching R1 to R3;

R3 and R7 are a pair of complementary nucleotide sequences having a free energy for association, over the entire length of the nucleotide sequence, from about 5.5 kcal/mole to 8.0 kcal/mole at a temperature from about 21° C to about 40° C and at a salt concentration from about 1 mM to about 100 mM, such that R3 and R7 only associate when R1 and R5 are bound to the target molecule;

R4 and R8 together comprise a detection means such that when R3 and R7 associate a detectable signal is produced;

R5 is an antibody epitope binding agent that binds to a second epitope on the target molecule; and

R6 is a non-nucleic acid flexible linker attaching R5 to R7.

Claim 110 (Previously presented) The molecular biosensor of claim 109, wherein the target molecule is selected from the group consisting of an analyte, a prion, a protein, a polypeptide, a nucleic acid, a lipid, a carbohydrate, a biomolecule, a macromolecular complex, a fungus, and a microbial organism.

Claim 111 (Previously presented) The molecular biosensor of claim 109, wherein the target molecule is a protein or polypeptide.

Claim 112 (Withdrawn) The molecular biosensor of claim 109, wherein R1 and R5 are each aptamers.

Claim 113 (Withdrawn) The molecular biosensor of claim 109, wherein R1 is a double stranded nucleic acid and R5 is an aptamer.

Claim 114 (Withdrawn) The molecular biosensor of claim 109, wherein R1 is an antibody and R5 is an aptamer.

Claim 115 (Withdrawn) The molecular biosensor of claim 109, wherein R1 is a double stranded nucleic acid and R5 is an antibody.

Claim 116 (Cancelled)

Claim 117 (Withdrawn) The molecular biosensor of claim 109, wherein R1 and R5 are each double stranded nucleic acids.

Claim 118 (Cancelled)

Claim 119 (Previously amended) The molecular biosensor of claim 109, wherein R2 forms a bond with each of R1 and R3 and R6 forms a bond with each of R5 and R7, wherein the free energy of the formed bonds is from about 12.0 kcal/mole to about 16.5 kcal/ mole.

Claim 120 (Previously presented) The molecular biosensor of claim 119, wherein the bonds are covalent bonds.

Claim 121 (Previously presented) The molecular biosensor of claim 109, wherein R2 and R6 are comprised of a bifunctional chemical crosslinker.

Claim 122 (Previously presented) The molecular biosensor of claim 109, wherein R2 and R6 are from 0 to 500 angstroms in length.

Claim 123 (Previously presented) The molecular biosensor of claim 109, wherein R2 and R6 are comprised of non-DNA polyethylene glycol and are from 0 to 500 angstroms in length.

Claim 124 (Previously presented) The molecular biosensor of claim 109, wherein R3 and R7 are from about 4 to about 15 nucleotides in length.

Claim 125 (Previously presented) The molecular biosensor of claim 109, wherein the R4 and R8 comprise a pair of molecules that transfer energy thereby producing a detectable signal.

Claim 126 (Previously presented) The molecular biosensor of claim 109, wherein the detection means is selected from the group consisting of FRET, fluorescence cross-correlation spectroscopy, flourescence quenching, fluorescence polarization, flow cytometry, scintillation proximity, luminescense resonance energy transfer, direct quenching, ground-state complex formation, chemiluminescence energy transfer, bioluminescence resonance energy transfer, excimer formation, colorimetric substrates detection, phosphorescence, electro-chemical changes, and redox potential changes.

Claim 127 (Currently amended) A molecular biosensor, the biosensor having two constructs, the constructs comprising:

R1-R2-R3-R4; and

R5-R6-R7-R8;

wherein:

R1 is an antibody epitope binding agent that binds to a first epitope on a target molecule ~~and is selected from the group consisting of an aptamer, an antibody, and double stranded nucleic acid~~;

R2 is a non-nucleic acid flexible linker attaching R1 to R3 by formation of a covalent bond with each of R1 and R3, wherein R2 comprises a bifunctional chemical crosslinker and is from 0 to 500 angstroms in length;

R3 and R7 are a pair of complementary nucleotide sequences from about 4 to about 15 nucleotides in length and having a free energy for association over the entire length of the nucleotide sequence from about 5.5 kcal/mole to 8.0 kcal/mole at a temperature from about 21° C to about 40° C and at a salt concentration from about 1 mM to about 100 mM, such that R3 and R7 only associate when R1 and R5 are bound to the target molecule;

R4 and R8 together comprise a detection means selected from the group consisting of FRET, fluorescence cross-correlation spectroscopy, flourescence quenching, fluorescence polarization, flow cytometry, scintillation proximity, luminescense resonance energy transfer, direct quenching, ground-state complex formation, chemiluminescence energy transfer, bioluminescence resonance energy transfer, excimer formation, colorimetric substrates detection, phosphorescence, electro-chemical changes, and redox potential changes;

R5 is an antibody epitope binding agent that binds to a second epitope on the target molecule ~~and is selected from the group consisting of an aptamer, an antibody, and double stranded nucleic acid~~; and

R6 is a non-nucleic acid flexible linker attaching R5 to R7 by formation of a covalent bond with each of R5 and R7, wherein R6 comprises a bifunctional chemical crosslinker and is from 0 to 500 angstroms in length.

Claim 128 (Withdrawn) A molecular biosensor, the biosensor having two aptamer constructs, the aptamer constructs comprising :

R1-R2-R3-R4; and

R5-R6-R7-R8;

wherein:

R1 is an aptamer that binds to a first epitope on a target molecule;

R2 is a flexible linker attaching R1 to R3;

R3 and R7 are a pair of complementary nucleotide sequences having a free energy for association from about 5.5 kcal/mole to about 8.0 kcal/mole at a temperature from about 21° C to about 40° C and at a salt concentration from about 1 mM to about 100 mM;

R4 and R8 together comprise a detection means such that when R3 and R7 associate a detectable signal is produced;

R5 is an aptamer that binds to a second epitope on the target molecule; and

R6 is a flexible linker attaching R5 to R7.

Claim 129 (Withdrawn) The molecular biosensor of claim 128, wherein the biosensor comprises:

R1-R2-R3-R4; and

R5-R6-R7-R8;

wherein:

R1 is an aptamer that binds to a first epitope on a target molecule;

R2 is a flexible linker attaching R1 to R3 by formation of a covalent bond with each of R1 and R3, wherein R2 comprises a bifunctional chemical crosslinker and is from 0 to 500 angstroms in length;

R3 and R7 are a pair of complementary nucleotide sequence from about 4 to about 15 nucleotides in length and having a free energy for association from about 5.5 kcal/mole to about 8.0 kcal/mole at a

temperature from about 21° C to about 40° C and at a salt concentration from about 1 mM to about 100 mM;

R4 and R8 together comprise a detection means selected from the group consisting of FRET, fluorescence cross-correlation spectroscopy, flourescence quenching, fluorescence polarization, flow cytometry, scintillation proximity, luminescense resonance energy transfer, direct quenching, ground-state complex formation, chemiluminescence energy transfer, bioluminescence resonance energy transfer, excimer formation, colorimetric substrates detection, phosphorescence, electro-chemical changes, and redox potential changes;

R5 is an aptamer that binds to a second epitope on the target molecule; and

R6 is a flexible linker attaching R5 to R7 by formation of a covalent bond with each of R5 and R7, wherein R6 comprises a bifunctional chemical crosslinker and is from 0 to 500 angstroms in length.

Claim 130 (Withdrawn) A molecular biosensor having three nucleic acid constructs, the nucleic acid constructs comprising:

R15-R14-R13-R9-R10-R11-R12;

R16-R17-R18-R19; and

R20-R21-R22-R23

wherein:

R9 is an epitope binding agent that binds to a first epitope on a target molecule;

R10 is a flexible linker attaching R9 to R11;

R11 and R22 are a first pair of complementary nucleotide sequences having a free energy for association from about 5.5 kcal/mole to about 8.0 kcal/mole at a temperature from about 21° C to about 40° C and at a salt concentration from about 1 mM to about 100 mM;

R12 and R23 together comprise a detection means such that when R11 and R22 associate a detectable signal is produced;

R13 is a flexible linker attaching R9 to R14;

R14 and R18 are a second pair of complementary nucleotide sequences having a free energy for association from about 5.5 kcal/mole to about 8.0 kcal/mole at a temperature from about 21° C to about 40° C and at a salt concentration from about 1 mM to about 100 mM;

R15 and R19 together comprise a detection means such that when R14 and R18 associate a detectable signal is produced;

R16 is an epitope binding agent that binds to a second epitope on a target molecule;

R17 is a flexible linker attaching R16 to R18;

R20 is an epitope binding agent that binds to a third epitope on a target molecule; and

R21 is a flexible linker attaching R20 to R22.

Claim 131 (Currently Amended) A molecular biosensor, the biosensor having two constructs, the constructs consisting of:

R1-R2-R3-R4; and

R5-R6-R7-R8;

wherein:

R1 is an antibody epitope binding agent that binds to a first epitope on a target molecule;

R2 is a non-nucleic acid flexible linker attaching R1 to R3;

R3 and R7 are a pair of complementary nucleotide sequences having a free energy for association from about 5.5 kcal/mole to 8.0 kcal/mole at a temperature from about 21° C to about 40° C and at a salt concentration from about 1 mM to about 100 mM, such that R3 and R7 only associate when R1 and R5 are bound to the target molecule;

R4 and R8 together comprise a detection means such that when R3 and R7 associate a detectable signal is produced;

R5 is an antibody epitope binding agent that binds to a second epitope on the target molecule; and

R6 is a non-nucleic acid flexible linker attaching R5 to R7.

Claim 132 (Previously Amended) The molecular biosensor of claim 131, wherein the target molecule is selected from the group consisting of an analyte, a prion, a protein, a polypeptide, a nucleic acid, a lipid, a carbohydrate, a biomolecule, a macromolecular complex, a fungus, and a microbial organism.

Claim 133 (Previously Presented) The molecular biosensor of claim 131, wherein the target molecule is a protein or polypeptide.

Claim 134 (Cancelled)

Claim 135 (Previously Presented) The molecular biosensor of claim 131, wherein R2 forms a bond with each of R1 and R3 and R6 forms a bond with each of R5 and R7, wherein the free energy of the formed bonds is from about 12.0 kcal/mole to about 16.5 kcal/ mole.

Claim 136 (Previously Presented) The molecular biosensor of claim 131, wherein the bonds are covalent bonds.

Claim 137 (Previously Presented) The molecular biosensor of claim 131, wherein R2 and R6 are comprised of a bifunctional chemical crosslinker.

Claim 138 (Previously Presented) The molecular biosensor of claim 131, wherein R2 and R6 are from 0 to 500 angstroms in length.

Claim 139 (Previously Presented) The molecular biosensor of claim 131, wherein R2 and R6 are comprised of non-DNA polyethylene glycol and are from 0 to 500 angstroms in length.

Claim 140 (Previously Presented) The molecular biosensor of claim 131, wherein R3 and R7 are from about 4 to about 15 nucleotides in length.

Claim 141 (Previously Presented) The molecular biosensor of claim 131, wherein the R4 and R8 comprise a pair of molecules that transfer energy thereby producing a detectable signal.

Claim 142 (Previously Presented) The molecular biosensor of claim 131, wherein the detection means is selected from the group consisting of FRET, fluorescence cross-correlation spectroscopy, flourescence quenching, fluorescence polarization, flow cytometry, scintillation proximity, luminescense resonance energy transfer, direct quenching, ground-state complex formation, chemiluminescence energy transfer, bioluminescence resonance energy transfer, excimer formation, colorimetric substrates detection, phosphorescence, electro-chemical changes, and redox potential changes.

Claim 143 (New) A molecular biosensor, the biosensor having two constructs, the constructs comprising:

R1-R2-R3-R4; and

R5-R6-R7-R8;

wherein:

R1 is an epitope binding agent that binds to a first epitope on a non-nucleic acid target molecule;

R2 is a non-nucleic acid flexible linker attaching R1 to R3;

R3 and R7 are a pair of complementary nucleotide sequences having a free energy for association, over the entire length of the

nucleotide sequence, from about 5.5 kcal/mole to 8.0 kcal/mole at a temperature from about 21° C to about 40° C and at a salt concentration from about 1 mM to about 100 mM;

R4 and R8 together comprise a detection means such that when R3 and R7 associate a detectable signal is produced;

R5 is an epitope binding agent that binds to a second epitope on the non-nucleic acid target molecule; and

R6 is a non-nucleic acid flexible linker attaching R5 to R7.

Claim 144 (New) The molecular biosensor of claim 143, wherein the target molecule is selected from the group consisting of an analyte, a prion, a protein, a polypeptide, a lipid, a carbohydrate, a biomolecule, a macromolecular complex, a fungus, and a microbial organism.

Claim 145 (New) The molecular biosensor of claim 143, wherein the target molecule is a protein or polypeptide.

Claim 146 (New) The molecular biosensor of claim 143, wherein R1 and R5 are each antibodies.

Claim 147 (New) The molecular biosensor of claim 143, wherein R2 forms a bond with each of R1 and R3 and R6 forms a bond with each of R5 and R7, wherein the free energy of the formed bonds is from about 12.0 kcal/mole to about 16.5 kcal/ mole.

Claim 148 (New) The molecular biosensor of claim 147, wherein the bonds are covalent bonds.

Claim 149 (New) The molecular biosensor of claim 143, wherein R2 and R6 are comprised of a bifunctional chemical crosslinker.

Claim 150 (New) The molecular biosensor of claim 143, wherein R2 and R6 are from 0 to 500 angstroms in length.

Claim 151 (New) The molecular biosensor of claim 143, wherein R2 and R6 are comprised of non-DNA polyethylene glycol and are from 0 to 500 angstroms in length.

Claim 152 (New) The molecular biosensor of claim 143, wherein R3 and R7 are from about 4 to about 15 nucleotides in length.

Claim 153 (New) The molecular biosensor of claim 143, wherein the R4 and R8 comprise a pair of molecules that transfer energy thereby producing a detectable signal.

Claim 154 (New) The molecular biosensor of claim 143, wherein the detection means is selected from the group consisting of FRET, fluorescence cross-correlation spectroscopy, flourescence quenching, fluorescence polarization, flow cytometry, scintillation proximity, luminescense resonance energy transfer, direct quenching, ground-state complex formation, chemiluminescence energy transfer, bioluminescence resonance energy transfer, excimer formation, colorimetric substrates detection, phosphorescence, electro-chemical changes, and redox potential changes.

Claim 155 (New) A molecular biosensor, the biosensor having two constructs, the constructs comprising:

R1-R2-R3-R4; and

R5-R6-R7-R8;

wherein:

R1 is an antibody epitope binding agent that binds to a first epitope on a target molecule;

R2 is a non-nucleic acid flexible linker attaching R1 to R3;

R3 and R7 are a pair of complementary nucleotide sequences having a free energy for association, over the entire length of the nucleotide sequence, from about 5.5 kcal/mole to 8.0 kcal/mole at a temperature from about 21˚ C to about 40˚ C and at a salt concentration from about 1 mM to about 100 mM;

R4 and R8 together comprise a detection means such that when R3 and R7 associate a detectable signal is produced;

R5 is an epitope binding agent that binds to a second epitope on target molecule; and

R6 is a non-nucleic acid flexible linker attaching R5 to R7.

Claim 156 (New) The molecular biosensor of claim 155, wherein the target molecule is selected from the group consisting of an analyte, a prion, a protein, a polypeptide, a lipid, a carbohydrate, a biomolecule, a macromolecular complex, a fungus, and a microbial organism.

Claim 157 (New) The molecular biosensor of claim 155, wherein the target molecule is a protein or polypeptide.

Claim 158 (New) The molecular biosensor of claim 155, wherein R1 and R5 are each antibodies.

Claim 159 (New) The molecular biosensor of claim 155, wherein R2 forms a bond with each of R1 and R3 and R6 forms a bond with each of R5 and R7, wherein the free energy of the formed bonds is from about 12.0 kcal/mole to about 16.5 kcal/ mole.

Claim 160 (New) The molecular biosensor of claim 155, wherein the bonds are covalent bonds.

Claim 161 (New) The molecular biosensor of claim 155, wherein R2 and R6 are comprised of a bifunctional chemical crosslinker.

Claim 162 (New) The molecular biosensor of claim 155, wherein R2 and R6 are from 0 to 500 angstroms in length.

Claim 163 (New) The molecular biosensor of claim 155, wherein R2 and R6 are comprised of non-DNA polyethylene glycol and are from 0 to 500 angstroms in length.

Claim 164 (New) The molecular biosensor of claim 155, wherein R3 and R7 are from about 4 to about 15 nucleotides in length.

Claim 165 (New) The molecular biosensor of claim 155, wherein the R4 and R8 comprise a pair of molecules that transfer energy thereby producing a detectable signal.

Claim 166 (New) The molecular biosensor of claim 155, wherein the detection means is selected from the group consisting of FRET, fluorescence cross-correlation spectroscopy, flourescence quenching, fluorescence polarization, flow cytometry, scintillation proximity, luminescense resonance energy transfer, direct quenching, ground-state complex formation, chemiluminescence energy transfer, bioluminescence resonance energy transfer, excimer formation, colorimetric substrates detection, phosphorescence, electro-chemical changes, and redox potential changes.